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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,673	10/07/2003	Jeff L. Ellsworth	02-21	5506

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ZymoGenetics, Inc.
1201 Eastlake Avenue East
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EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/680,673	ELLSWORTH, JEFF L.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-26* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1–26 are pending.

Applicant's election of group II, claims 9–26, the species high molecular weight hyaluronans, and the species solution in the reply filed on 11/06/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1–8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/06/2006.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 9, 11, 13 and 15-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Yayon (U. S. Patent No. 7,009,039).

Yayon discloses a freeze-dried, biocompatible, biodegradable matrix of plasma-derived proteins that is useful in methods for regenerating and/or repairing various tissues in vivo (paragraph bridging columns 7-8). The matrix can be utilized as an implantable scaffold in reconstructive surgery methods for regenerating and/or repairing tissue that have been damaged for example by trauma, surgical procedures or disease (column 8, full paragraph 1). Scaffold

applications include the regeneration of cartilaginous tissues (column 8, full paragraph 2). Also included is the introduction into the sponge of an auxiliary component which is a bioactive agent selected from growth factors, cytokines, enzymes, anti-microbials, anti-inflammatory agents (column 9, full paragraph 1). In other embodiments the matrix includes hyaluronic acid (column 12, last full paragraph). Bioactive agents, such as FGF18, may be included in the matrix in order to enhance a therapeutic effect, such as cartilage healing. Incorporation of such agents into the sponge of the present invention provides a slow-release or sustained-release mechanism. See column 13, full paragraph 1. In the reconstruction of structural tissues like cartilage and bone, tissue shape is integral to function, requiring the molding of the matrix into three dimensional configuration articles of varying thickness and shape (column 11, full paragraph 3). The examiner construes Yayon's implantation as "administering into a synovial cavity." Furthermore, a chemical composition and its properties are inseparable. Therefore, the properties applicant discloses and/or claims, i.e. "increasing chondrocyte proliferation", are necessarily present in Yayon's FGF-18/hyaluronic acid-supplemented matrix.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 12–13, 17–18, 20–22 and 24–26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yayon (U. S. Patent No. 7,009,039) as applied to claims 9, 11, 13 and 15-16 above and further in view of Kikuchi (Osteoarthritis Cartilage. 1996 Jun;4(2):99-110).

Yayon teaches a method for increasing chondrocyte proliferation in a joint of a mammal in need thereof comprising the step of administering into a synovial cavity a pharmaceutically acceptable admixture comprising FGF18 and hyaluronic acid, where said admixture is a time-release formulation, as discussed above. Yayon does not teach, only in the sense that Yayon does not anticipate, said method wherein said admixture further comprises high molecular weight hyaluronans, or said method further comprising the steps of allowing growth of new cartilage tissue and surgically contouring the new cartilage surface.

Kikuchi teaches that osteoarthritis is a common joint disease, characterized by degenerative changes in articular cartilage (page 99, left column, full paragraph 1). Kikuchi suggest that intra-articular administration of higher molecular weight HA is more effective than lower molecular weight HA in inhibiting cartilage degeneration in early OA (Abstract). Kikuchi does not teach a method for increasing chondrocyte proliferation in a joint of a mammal in need thereof comprising the step of administering into a synovial cavity a pharmaceutically acceptable admixture comprising FGF18 and hyaluronic acid. However, it is fair to say that Kikuchi recognizes the molecular weight of HA as a result effective variable and that it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use high molecular weight HA because higher molecular weight HA is more effective than lower molecular weight HA.

It would have been further obvious to one of ordinary skill in the art at the time of Applicants' invention to allow growth of new cartilage tissue and surgically contour the new cartilage surface, with a reasonable expectation of success. One of ordinary skill in the art would

be motivated to make this modification because in the reconstruction of structural tissues like cartilage, tissue shape is integral to function.

It would have been further obvious to one of ordinary skill in the art at the time of applicants invention to treat osteoarthritis in a mammal, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because osteoarthritis is a common joint disease, characterized by degenerative changes in articular cartilage.

The invention is prima facie obvious over the prior art.

Claims 9–10, 13–14, 18–19 and 22–23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yayon (U. S. Patent No. 7,009,039) as applied to claims 9, 11, 13 and 15-16 above and further in view of Kikuchi (Osteoarthritis Cartilage. 1996 Jun;4(2):99-110) as applied to claims 9, 12–13, 17–18, 20–22 and 24–26 above and further in view of MacPhee (U. S. Patent No. 6,054,122).

Yayon in view of Kikuchi teach a method of increasing chondrocyte proliferation or treating osteoarthritis, as discussed above. Yayon in view of Kikuchi do not teach injection of a solution of Yayon's matrix.

MacPhee discloses tissue sealants (TS), such as fibrin glue (FG), made from the mixing of topical fibrinogen complex (TFC), human thrombin and calcium chloride. Varying the concentration of the TFC has the most significant effect upon the density of the final FG matrix. Varying the concentration of the thrombin has an insignificant effect upon the total protein concentration of the final FG, but has a profound effect upon the time required for the polymerization of the fibrinogen component of the TFC into fibrin. While this effect is well known, it is not generally appreciated that it may be used to maximize the effectiveness of the FG, when it is used alone or supplemented. Because of this effect one can alter the time between the mixing of the FG components and the setting of the FG. Thus, one can allow the FG to flow more freely into deep crevices in a wound, permitting it to fill the wound completely before the

FG sets. Alternatively, one can allow the FG to set quickly enough to prevent it from exiting the wound site, especially if the wound is leaking fluid under pressure (i.e., blood, lymph, intercellular fluid, etc). This property is also important to keep the FG from clogging delivery devices with long passages, i.e., catheters, endoscopes, etc., which is important to allow the application of the FG or supplemented FG to sites in the body that are only accessible by surgery. This effect is also important in keeping the insoluble supplements in suspension and preventing them from settling in the applicator or in the tissue site. TFC is a lyophilized mixture of human plasma proteins which have been purified and virally inactivated. When reconstituted TFC contains: 100-130 mg total protein/ml and a minimum of 80% of total protein as fibrinogen. See column 10, lines 28-61. For site-directed cartilage induction the supplemented TS can be implanted into the body of the recipient in the liquid form as the TS is mixed and polymerizes (column 66, full paragraph 3). MacPhee does not teach a method for increasing chondrocyte proliferation or treating osteoarthritis in a joint of a mammal in need thereof comprising the step of administering into a synovial cavity a pharmaceutically acceptable admixture comprising FGF18 and hyaluronic acid.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to increase chondrocyte proliferation or treat osteoarthritis in a joint of a mammal in need thereof by administering into a synovial cavity a pharmaceutically acceptable admixture comprising FGF18 and hyaluronic acid, as taught by Yayon further in view of Kikuchi, and to modify that teaching by injecting a liquid form of the admixture comprising FGF18 and hyaluronic acid, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to maximize the effectiveness of the FG, when it is supplemented. Because of this effect one can alter the time between the mixing of the FG components and the setting of the FG. Thus, one can allow the FG to flow more freely into deep crevices in a wound, permitting it to fill the wound completely before the FG sets. Alternatively, one can allow the FG to set quickly enough to prevent it from exiting the wound site, especially if the wound is leaking fluid under pressure (i.e., blood, lymph, intercellular fluid, etc). This property is also important to keep the FG from clogging delivery devices with long passages, i.e., catheters, endoscopes, etc., which is important to allow the

application of the FG or supplemented FG to sites in the body that are only accessible by surgery. The examiner construes "a liquid form" as "a solution."

The invention is prima facie obvious over the prior art.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
FEBRUARY 5, 2007